

WHAT IS CLAIMED:

1. A method of modulating apoptosis in a cell, comprising the step of administering to the cell an agent that modulates the amount or activity of Survivin in the cell.
2. The method of claim 1, wherein the level of apoptosis is increased by decreasing the amount or activity of Survivin in the cell.
3. The method of claim 1, wherein the level of apoptosis is decreased by increasing the amount or activity of Survivin in the cell.
4. A method of inhibiting apoptosis in a cell, comprising the step of administering to the cell a Survivin polypeptide, Survivin polypeptide fragment or an apoptosis-inhibiting peptidomimetic thereof in an amount effective to inhibit apoptosis in the cell.
5. A method of inhibiting apoptosis in a cell, comprising the step of administering to the cell a transgene encoding a Survivin polypeptide or Survivin polypeptide fragment thereof, the transgene being effective to cause expression of the Survivin polypeptide or fragment thereof in an amount effective to inhibit apoptosis in the cell.
6. A method of increasing apoptosis in a cell, comprising the step of administering to the cell an agent that decreases the apoptosis-inhibiting activity of the Survivin polypeptide present in the cell, in an amount that is effective to increase the level of apoptosis in the cell.

- 75 -

7. The method of claim 6, wherein said agent is a polypeptide comprising the sequence EGWEPDDDDPIEEHKKHSSGC, its conservatively substituted homologs or small molecule peptidomimetics thereof.

5 8. A method of increasing the level of apoptosis in a cell, comprising the step of administering to the cell an agent that increases the transcription of the sense strand of EPR-1, in an amount effect to inhibit the translation of mRNA encoding a Survivin polypeptide, thereby decreasing the transcription of the Survivin polypeptide and increasing the level of apoptosis in the cell.

10 9. An isolated nucleic acid molecule that encodes the amino acid sequence depicted in Figure 10, allelic variants of the amino acid sequence of Figure 10, and fragments thereof that are effective to inhibit apoptosis.

15 10. The isolated nucleic acid molecule of claim 9, wherein said nucleic acid molecule is operably linked to one or more expression control elements.

20 11. The isolated nucleic acid molecule of claim 9, wherein said nucleic acid molecule is included in a vector.

25 12. An isolated nucleic acid molecule that encodes a member of the Survivin family of proteins, wherein said nucleic acid molecule hybridizes to a nucleic acid molecule of claim 9 under conditions of sufficient stringency to produce a clear signal.

30 13. A host cell transformed to contain the nucleic acid molecule of claim 9.

14. The host cell of claim 13, wherein said host is selected from the group consisting of prokaryotic hosts and eukaryotic hosts.

- 76 -

15. A method for producing a Survivin protein comprising the step of culturing a host transformed with the nucleic acid molecule of claim 11 under conditions in which the Survivin protein is expressed.

5 16. The method of claim 15, wherein said host is selected from the group consisting of prokaryotic hosts and eukaryotic hosts.

Sub 12 17. An isolated polypeptide comprising the amino acid sequence depicted in Figure 10, allelic variants thereof and fragments thereof that retain the ability to
10 inhibit cellular apoptosis.

18. A polypeptide comprising the sequence
EGWEPDDDDPIEEHKKHSSGC, its conservatively substituted homologs and small molecule peptidomimetics thereof.

15

19. A monoclonal antibody that binds to the polypeptide, allelic variants thereof and fragments thereof that retain the ability to inhibit cellular apoptosis of claim 17.

20 20. The monoclonal antibody of claim 19 which has been humanized.

21. A method for reducing the severity of a pathological state mediated by Survivin comprising the step of reducing Survivin expression or activity.

25 22. The method of claim 21 wherein said pathological state is caused by abnormal cell growth.

23. The method of claim 21 wherein said Survivin expression is reduced by contacting affected cells with an RNA molecule that is complementary to a
30 Survivin encoding mRNA molecule.

24. The method of claim 21, wherein said Survivin activity is reduced by blocking the intracellular interaction of Survivin with a Survivin binding partner comprising the step of contacting said Survivin with an agent that blocks the binding
5 of Survivin to said binding partner.

25. The method of claim 24 wherein said agent blocks the binding of said Survivin to said binding partner by selectively binding to Survivin.

10 26. The method of claim 25 wherein said agent blocks the binding of said Survivin to said binding partner by selectively binding to the binding partner.

27. The method of claim 26 wherein said agent is a polypeptide fragment of Survivin.
15

28. The method of claim 26 wherein said agent comprises the polypeptide sequence EGWEPDDDPIEEHKKHSSGC, its conservatively substituted homologs and small molecule peptidomimetics thereof.

20 29. A method for identifying agents that block the interaction of Survivin with a Survivin binding partner comprising the steps of:

- a) incubating Survivin, or a fragment thereof, or a polypeptide comprising the sequence EGWEPDDDPIEEHKKHSSGC, and a binding partner, or a fragment thereof, with an agent to be tested, and
25 b) determining whether said agent blocks the binding of Survivin to said Survivin binding partner.

30. A method to assay for the presence of Survivin comprising the step of determining whether a Survivin protein is expressed by a sample.
30

- 78 -

31. The method of claim 30, wherein said sample is selected from the group consisting of a tissue biopsy, stool, blood, urine and saliva.

32. The method of claim 30 further comprising the steps of:

- 5
- a) preparing an extract of the cells in said sample, and
 - b) examining the proteins of said cell extract to determine the presence of a Survivin protein.

33. The method of claim 30 further comprising the steps of:

- 10
- a) preparing an extract of the cells in said sample, and
 - b) examining the mRNA of said cell extract to determine the presence of a Survivin encoding mRNA.

34. The method of claim 30 wherein said method is used to determine the growth potential of a tumor cell by correlating the level of Survivin expression with control samples to indicate tumor growth potential.

35. A method of detecting or monitoring the stage or progression of a cancer comprising the steps of:

- 20
- obtaining a biological fluid sample from a subject;
 - contacting said sample with a monoclonal antibody that recognizes and binds to Survivin; and
 - determining whether the monoclonal antibody recognizes and binds to Survivin in said sample, the presence of Survivin thereby predicting the presence of
- 25 cancer.

36. The method of claim 35, wherein the presence of Survivin predicts late stage neoplastic disease.

- 79 -

37. A method for preserving the growth of cells in culture, comprising the step of contacting the cells with an amount of Survivin that is effective to reduce apoptosis.

5 38. A kit for detecting the presence of Survivin in a sample, comprising an antibody that binds specifically to Survivin and reagents to detect the antibody-Survivin binding pair.

10 39. A therapeutic vaccine that modulates the level of Survivin-mediated apoptosis in a host.

40. The vaccine of claim 39, comprising a component that decreases the activity of Survivin in the host, selected from the group of components consisting of: (1) Survivin protein or fragments thereof sufficient to evoke a cellular mediated response, (2) a DNA molecule that is antisense to Survivin mRNA or portions thereof sufficient to inhibit translation of Survivin, (3) the sense DNA strand of EPR-1 acid or portions thereof sufficient to inhibit translation of Survivin.

41. A method of prophylactic or preventative anti-apoptotic therapy, comprising the administration of a Survivin polypeptide, Survivin polypeptide fragment, an apoptosis-inhibiting peptidomimetic thereof, a transgene encoding a Survivin polypeptide, or a transgene encoding a Survivin polypeptide fragment to a subject before the occurrence of a disease phenotype associated with cell apoptosis.

25 42. The method of claim 41, wherein the disease phenotype is a diminished T cell count in a subject infected with HIV.

43. The method of claim 41, wherein the disease phenotype is a degenerative disease.

30

51. The method of claim 50 wherein said agent is a fragment of Survivin.

52. The method of claim 50 wherein said agent comprises the polypeptide sequence EGWEPDDDDPIEEHKKHSSGC, its conservatively substituted homologs and small molecule peptidomimetics thereof.

5 53. A method of inhibiting or reversing reperfusion injury in a subject comprising the step of administering to subject in need thereof a Survivin polypeptide, an apoptosis-inhibiting Survivin polypeptide fragment or an apoptosis-inhibiting peptidomimetic thereof.

10 54. The method of claim 53 wherein said step of administering comprises local administration at the site of injury.

15 55. A method for inhibiting or preventing tissue or organ transplant rejection, comprising a local administration of a Survivin polypeptide, an apoptosis-inhibiting Survivin polypeptide fragment, an apoptosis-inhibiting peptidomimetic thereof, a transgene encoding a Survivin polypeptide or a transgene encoding an apoptosis-inhibiting Survivin polypeptide fragment to the tissue or organ or to a site proximal to the transplant.

20 56. A method for enhancing viability of organs and tissues prior to their transplantation into a subject, comprising the perfusion of the organs or tissues with a a Survivin polypeptide, an apoptosis-inhibiting Survivin polypeptide fragment, or an apoptosis-inhibiting peptidomimetic thereof.

25 57. The method of claim 56, wherein said transgene is delivered via a viral vector.

58. The method of claim 57 wherein said vector is replication defective.

59. The method of ~~claim 56~~ wherein said transgene is delivered as a naked nucleic acid.

add 7
C13

with
D₆